
Self-Reported Exposure to Pesticides and Radiation Related to Pregnancy Outcome—Results from National Natality and Fetal Mortality Surveys

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Synopsis

Although fetal development is known to be sensitive to environmental agents, relatively little

epidemiologic research has addressed this concern. Effects on pregnancy outcome of self-reported parental exposure to pesticides and to radiation were examined using data from the National Natality and Fetal Mortality Surveys, large national probability samples of live births and stillbirths occurring in 1980. In case-control analyses, maternal exposure to pesticides at home or work was associated with increased risk of stillbirth (odds ratios (ORs) = 1.5-1.6). Paternal pesticide exposure was associated with stillbirth (ORs = 1.2-1.4) and delivery of small-for-gestational-age infants (ORs = 1.4-2.0). A small increased risk of stillbirth (OR = 1.3) was found in relation to either parent's reported exposure to radiation. In spite of limitations in the quality of exposure data and the possibility of biased recall related to pregnancy outcome, associations of reported pesticide exposure to either parent with risk of stillbirth and small-for-gestational-age infants warrant further evaluation.

GIVEN THE KNOWN VULNERABILITY of fetal development to environmental influences and experimental evidence for such effects (1), the impact of environmental exposures on reproductive health warrants close examination. Available epidemiologic data mostly concern miscarriage and birth defects (2,3). Nonetheless, detrimental effects on birth weight from maternal exposure to anesthetic gases (4), selected manufacturing occupations (5), and hazardous wastes have been reported (6). Stillbirth has been reported to be associated with maternal employment in the textile (5,7) and leather industries (8,9), and with lead and cadmium exposure (10). Few studies have considered paternal exposure, but an association of stillbirth with employment in textile machining (7) and copper smelting has been suggested (11). Laboratory studies have demonstrated that mechanisms exist by which paternal exposures can adversely affect fetal development (12,13).

Given this limited knowledge, the analysis of available data provides an efficient opportunity to extend our understanding. The National Natality

and Fetal Mortality Surveys (14) provide data on self-reported parental exposures to pesticides and radiation, detailed birth outcome data, and information on an extensive array of potential confounders suitable for addressing these concerns.

Methods

The National Natality Survey and National Fetal Mortality Survey were probability samples of 1980 U.S. live births ($N = 9,941$) and stillbirths ($N = 6,386$). Stillbirths were defined by a gestational age of 28 weeks or greater or, if gestational age was missing, by a weight of at least 1,000 grams (14).

From the initial samples, births to unmarried mothers and plural births or births of unknown plurality were excluded. In addition, 44 percent of live births and 46 percent of stillbirths were omitted due to nonresponse (14), since the exposure items of interest were not included in the telephone interview administered to some of those who did not respond to the mailed questionnaire. Additional losses were incurred because of missing birth

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weight or gestational age among live births. Analyses of workplace exposures omitted respondents who had not worked in the 12 months before delivery (accounting for different numbers of mothers and fathers). Adjusted analyses omitted subjects who were missing data for any of the potential confounders.

All interview and questionnaire data were obtained following delivery, so that subjects were aware of their pregnancy outcome. The data were analyzed as a series of case-control studies. Final counts after making the exclusions were as follows:

Type of birth	Mother	Father
Stillbirths	2,025	1,948
Live birth controls	3,756	3,625
Preterm births (less than 37 weeks gestation)	378	365
Term controls	2,706	2,612
Very low birth weight (1,500 grams or less)	91	81
Normal weight births (more than 2,500 grams)	3,187	3,072
Small for gestational age births (less than the 10th percentile of weight for gestational age)	235	233
Appropriate for gestational age controls	2,797	2,697

As in all case-control studies, the sampling fractions are arbitrary (16), and it is not necessary to consider the complex sampling scheme used in these surveys.

The following questions were asked (exclusively of mothers) to assess exposure (14):

During the 12 months before your delivery, (were you/was the father) exposed to chemicals used to kill insects, rodents, weeds, or fungi?

(If yes) Where did this exposure occur?

At home, In the area where (I/he) lived, At (my/his) job, Other

In (your/the father's) job, did (you/he) work with or have exposure to radiation—radioactive isotopes or elements (Examples: microwave, X-rays, fluoroscopic equipment, lasers)?

Potential confounders were examined for their association with the pregnancy outcomes, and those which were strongly associated were included in the statistical analyses, as described in footnotes to the tables. For several confounders, the high-risk stratum had relatively few observations (for example, absence of prenatal care), so that restriction rather than stratification was used as the method of control. Mantel-Haenszel adjusted odds ratios (OR) (17) and test-based 95 percent confidence intervals (CI) (18) were calculated through stratified analysis.

Results

Stillbirth risk was elevated by 50–60 percent in relation to mothers' reported pesticide exposure, regardless of the source, with a smaller increase for reported radiation exposure at work (table 1). In contrast, preterm delivery was unrelated to any of the self-reported exposures. Very low birth weight was increased with pesticide exposure at work (OR = 2.4, 95 percent CI = 1.1–5.0). Other sources of exposure (pesticides near residence, radiation at work) could not be examined due to the small number of very low birth weight cases. Risk of being small-for-gestational-age was somewhat elevated with pesticide exposure at home (OR = 1.5) and to a lesser extent at work (OR = 1.2).

Father's exposure followed a similar pattern (table 2), with more modest associations (ORs = 1.2–1.4) found for stillbirth in relation to all sources of reported pesticide and radiation exposure. None of the exposures were predictive of preterm delivery. For very low birth weight, small decreases in risk were associated with pesticide exposures at home or work, and an increased risk (OR = 1.5) was found for radiation exposure at work. As with mothers, the strongest associations were found for small-for-gestational age births. A twofold increased risk was associated with pesticide exposure in the area of the residence, with odds ratios of 1.3–1.5 for other sites of pesticide exposure.

Discussion

This analysis identified modest associations of both maternal and paternal pesticide exposure with risk of stillbirth and small-for-gestational-age births. There was also some evidence linking maternal exposure to pesticides at work and paternal exposure to radiation at work to cases of very low birth weight. In addition, associations were ob-

Table 1. Mothers' self-reported exposures and pregnancy outcome: number of cases and adjusted odds ratios

Exposure	Stillbirth			Preterm delivery			Very low birth weight			Small for gestational age		
	Number of cases	Adjusted odds ratios ¹	95 percent CI	Number of cases	Adjusted odds ratios ²	95 percent CI	Number of cases	Adjusted odds ratios ³	95 percent CI	Number of cases	Adjusted odds ratios ⁴	95 percent CI
Pesticides, herbicides, and fungicides:												
Not exposed.....	1,497	1.0	...	299	1.0	...	72	1.0	...	175	1.0	...
Exposed in area of residence.....	76	1.6	1.1–2.2	12	0.9	0.4–2.0	0	9	1.1	0.5–2.4
Exposed in home ...	416	1.5	1.3–1.7	59	1.0	0.7–1.4	10	0.7	0.3–1.5	51	1.5	1.1–2.1
Exposed at job.....	137	1.6	1.3–2.1	21	1.1	0.6–2.1	9	2.4	1.1–5.0	11	1.2	0.6–2.3
Radiation on job:												
Not exposed.....	1,552	1.0	...	292	1.0	...	78	1.0	...	165	1.0	...
Exposed.....	157	1.3	1.0–1.6	17	0.8	0.4–1.4	2	10	0.8	0.4–1.5

¹ Adjusted by stratified analysis controlling for child's race and mother's previous miscarriages; restricted to mothers who received prenatal care, mother's age under 40, mother's drinking none, low, or medium, no previous stillbirths.

² Adjusted by stratified analysis controlling for child's race and maternal smoking (none, 1 or more cigarettes per day); restricted to women who received prenatal care, mother's age 20 or older, 0 or 1 previous miscarriage, and no previous induced abortion.

³ Adjusted by stratified analysis controlling for child's race, maternal smoking (none, 1 or more cigarettes per day) and month prenatal care began; restricted to women with more than a 12-month interval since previous live birth.

⁴ Adjusted by stratified analysis controlling for child's race, sex, and maternal smoking (none, 1 or more cigarettes per day); restricted to mothers age 20 or older.

Table 2. Fathers' exposures and pregnancy outcome: number of cases and adjusted odds ratios

Exposure	Stillbirth			Preterm delivery			Very low birth weight			Small for gestational age		
	Number of cases	Adjusted odds ratios ¹	95 percent CI	Number of cases	Adjusted odds ratios ²	95 percent CI	Number of cases	Adjusted odds ratios ³	95 percent CI	Number of cases	Adjusted odds ratios ⁴	95 percent CI
Pesticide, herbicides, and fungicides:												
Not exposed.....	1,340	1.0	...	262	1.0	...	70	1.0	...	158	1.0	...
Exposed in area of residence.....	85	1.4	1.0–1.9	14	0.9	0.4–1.9	2	16	2.0	1.1–3.6
Exposed in home ...	457	1.3	1.1–1.5	71	1.0	0.7–1.4	11	0.6	0.3–1.3	62	1.5	1.1–2.0
Exposed at job....	197	1.2	1.0–1.5	35	1.1	0.7–1.8	6	0.7	0.3–1.8	24	1.4	0.9–2.3
Radiation on job:												
Not exposed.....	1,927	1.0	...	345	1.0	...	75	1.0	...	204	1.0	...
Exposed.....	144	1.3	1.0–1.6	20	0.9	0.5–1.7	8	1.5	0.6–3.4	14	1.0	0.5–1.9

¹ Adjusted by stratified analysis controlling for child's race and mother's previous miscarriages; restricted to mothers who received prenatal care, mother's age under 40, mother's drinking none, low, or medium, no previous stillbirths.

² Adjusted by stratified analysis controlling for child's race and maternal smoking (none, 1 or more cigarettes per day); restricted to women who received prenatal care, mother's age 20 or older, 0 or 1 previous miscarriage, and no previous induced abortion.

³ Adjusted by stratified analysis controlling for child's race, maternal smoking (none, 1 or more cigarettes per day) and month prenatal care began; restricted to women with more than a 12-month interval since previous live birth.

⁴ Adjusted by stratified analysis controlling for child's race, sex, and maternal smoking (none, 1 or more cigarettes per day); restricted to mothers age 20 or older.

served between reported exposure of either parent to radiation and stillbirth. None of these exposures of either parent were predictive of preterm delivery.

Given the public's concerns regarding pesticide exposure and adverse health effects on reproduction, few epidemiologic studies have addressed this association (1,3). Toxicological studies (2) support a range of potential reproductive health consequences of pesticide exposures, though they do not generate predictions of a specific effect on pregnancy outcomes.

High doses of ionizing radiation can affect stillbirth and possibly other pregnancy outcomes

(3), though the presumably low-level occupational exposures assessed in this study have received little attention. In this analysis, reported paternal radiation exposure was weakly associated with stillbirth (OR = 1.3) and very low birth weight (OR = 1.5). The known mutagenic effects of ionizing radiation (19) make a sperm-mediated influence on fetal development plausible. The recent observations relating ionizing radiation exposure to neural tube defects (20,21) could also be interpreted as reflections of such a process.

The most important limitation in this analysis is the quality of self-reported exposure data. Relative

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to the actual exposures received, self-report is likely to produce substantial misclassification which, if nondifferential with respect to birth outcome, would bias the odds ratios towards the null (22). Since exposure data were not collected until after the delivery, there is also a possibility of recall bias in that women who had adverse outcomes might overreport or report more completely potentially hazardous exposures. Selective recall might be expected to be strongest for the most severe outcomes (stillbirth, very low birth weight), consistent with the increased risks found in this study. Although biased recall could not be addressed directly, available data to validate occupational exposures (as discussed subsequently) suggest that this did not occur.

In addition to the uncertainty in mothers' reports of their own exposure, their perceptions of the father's exposure may be more prone to error. Occupational exposures have been found to be reported by spouses with reasonable accuracy (23,24), especially when exposures were inferred from the job title (24). Nonetheless, the loss of information about fathers' exposures relative to mothers' should be noted in comparing the strengths of association with pregnancy outcome. Regardless of the actual accuracy of self-reported exposure to pesticides, the reporting of exposures in the home and yard would be highly correlated for the mothers and fathers. The heterogeneity of exposures potentially reflected by pesticides and radiation and the uncertainty regarding the time of exposure would further attenuate any underlying etiologic associations. For example, the question on radiation could have been interpreted to include all frequencies of electromagnetic radiation, which would not be expected to produce similar effects on birth outcome.

Although there is no direct way of evaluating the accuracy of self-reported exposures (for example, by comparison with biological markers of exposure

or radiation film badges), the self-reported occupational exposures were compared with exposures imputed according to a job-exposure linkage system (25). Self-reported occupational exposures of mothers and fathers to pesticides were compared to imputed exposures to alicyclic halogens through the job-exposure matrix. Similarly, self-reported radiation exposures were compared to imputed ionizing radiation exposures. For discussion purposes only, the imputed exposures were treated as the "gold standard." Though such imputed exposures are highly imperfect, they assign exposures objectively and should be free from recall bias.

Overall, in the study by Hoar and coworkers (25) the sensitivity of self-reported exposure was low (typically 10–20 percent) though specificity was high (approximately 90 percent). Nonetheless, the likelihood that each exposure was reported was markedly greater if that exposure was imputed using the job-exposure linkage system than if it was not. Most importantly, the quality of classification was quite similar for cases and controls. Using formulas for correcting odds ratios for misclassification (26), the observed odds ratios for self-reported occupational exposure were compared with the odds ratios corrected for misclassification (again, using the imputed exposures as the criterion of validity). None of the corrected odds ratios differed by more than 10 percent from the observed values, indicating that differential misclassification for cases and controls is unlikely to account for the reported associations with occupational exposures.

Other limitations result from the modest size of the study group (especially for cases of very low birth weight), potential residual confounding by unmeasured or inadequately measured risk factors, and limited generalizability because of the surveys' restriction to married women who responded to the survey and provided complete data. Nonresponse was sizable, reducing confidence in the results, although differential response by both exposure and disease status would be required to bias the reported odds ratios (27). In order to account for the elevated risks, one would have to invoke selective participation by exposed parents of cases relative to unexposed parents of cases or exposed controls relative to unexposed controls, which seems unlikely.

The advantages of the National Natality and Fetal Mortality Surveys include the large study sample, carefully conducted national probability sampling, and detailed data on pregnancy outcome and potential confounding factors. These results

should encourage continued evaluation of the effect of parental exposure to pesticides (and to a lesser extent, paternal exposure to ionizing radiation) on pregnancy outcomes, especially stillbirth and delivery of small-for-gestational-age infants.

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